



## Improved Devices for Collecting Sweat for Chemical Analysis

**Unlike prior devices, these would enable measurement of volumes of specimens.**

*Lyndon B. Johnson Space Center, Houston, Texas*

Improved devices have been proposed for collecting sweat for biochemical analysis — especially for determination of the concentration of  $\text{Ca}^{2+}$  ions in sweat as a measure of loss of Ca from bones. Unlike commercially available sweat-collection patches used previously in monitoring osteoporosis and in qualitative screening for some drugs, the proposed devices would not allow evaporation of the volatile chemical components (mostly water) of sweat. Moreover, the proposed devices would be designed to enable determination of the volumes of collected sweat. From these volumes and the quantities of  $\text{Ca}^{2+}$  and/or other analytes as determined by other means summarized below, one could determine the concentrations of the analytes in sweat.

A device according to the proposal would be flexible and would be worn like a commercial sweat-collection patch. It would be made of molded polydimethylsiloxane (silicone rub-

ber) or other suitable material having properties that, for the purpose of analyzing sweat, are similar to those of glass. The die for molding the silicone rubber would be fabricated by a combination of lithography and electroplating. The die would reproducibly form, in the silicone rubber, a precisely defined number of capillary channels per unit area, each channel having a precisely defined volume. Optionally, electrodes for measuring the  $\text{Ca}^{2+}$  content of the sweat could be incorporated into the device.

The volume of sweat collected in the capillary channels of the device would be determined from (1) the amount of light or radio waves of a given wavelength absorbed by the device and (2) the known geometry of the array of capillary channels. Then, in one of two options, centrifugation would be performed to move the sweat from the capillary tubes to the region containing

the electrodes, which would be used to measure the  $\text{Ca}^{2+}$  content by a standard technique. In the other option, centrifugation would be performed to remove the sweat from the device to make the sweat available to other analytical instruments for measuring concentrations of substances other than  $\text{Ca}^{2+}$ .

*This work was done by Daniel L. Feeback of Johnson Space Center and Mark S. F. Clarke of the University of Houston. Further information is contained in a TSP (see page 1).*

*In accordance with Public Law 96-517, the contractor has elected to retain title to this invention. Inquiries concerning rights for its commercial use should be addressed to:*

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## Tissue Photolithography

**This method for extracting pure DNA from single cancer cells enables high-specificity cancer identification.**

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Tissue lithography will enable physicians and researchers to obtain macromolecules with high purity (>90 percent) from desired cells in conventionally processed, clinical tissues by simply annotating the desired cells on a computer screen. After identifying the desired cells, a suitable lithography mask will be generated to protect the contents of the desired cells while allowing destruction of all undesired cells by irradiation with ultraviolet light. The DNA from the protected cells can be used in a number of downstream applications including DNA sequencing. The purity (i.e., macromolecules isolated from specific cell types) of such specimens will greatly enhance the value and information of downstream applications.

In this method, the specific cells are isolated on a microscope slide using photolithography, which will be faster, more specific, and less expensive than current methods. It relies on the fact that many biological molecules such as DNA are photosensitive and can be destroyed by ultraviolet irradiation. Therefore, it is possible to "protect" the contents of desired cells, yet destroy undesired cells. This approach leverages the technologies of the microelectronics industry, which can make features smaller than 1  $\mu\text{m}$  with photolithography.

A variety of ways has been created to achieve identification of the desired cell, and also to designate the other cells for destruction. This can be accomplished through chrome masks, direct laser writ-

ing, and also active masking using dynamic arrays. Image recognition is envisioned as one method for identifying cell nuclei and cell membranes. The pathologist can identify the cells of interest using a microscopic computerized image of the slide, and appropriate custom software.

In one of the approaches described in this work, the software converts the selection into a digital mask that can be fed into a direct laser writer, e.g. the Heidelberg DWL66. Such a machine uses a metalized glass plate (with chrome metallization) on which there is a thin layer of photoresist. The laser transfers the digital mask onto the photoresist by direct writing, with typical best resolution of 2  $\mu\text{m}$ . The plate is